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Synthesis and Herbicidal Activity of 1,4-Benzoxazin-3-one Sulfonylureas

Janet E. Anderson, Stephen Bell, Wayne M. Best, Peter F. Drygala, Keith G. Watson*

ICI Australia, Research Group, Ascotvale, Victoria 3032, Australia

& Ian B. Bryan

Zeneca Agrochemicals, Jealotts Hill Research Station, Bracknell, Berkshire RG12 6EY, UK

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Abstract: A series of 1,4-benzoxazin-3-ones with a sulfonylurea group attached at either the 5 or 8 position have been synthesised and found to show moderate herbicidal activity. Similarly, a series of 1,4-benzothiazin-3-ones, including some of the related *S*-oxides and *S*-dioxides, with a sulfonylurea group linked at the 8 position, have been prepared and been found to be herbicidal. In both series of compounds many substituent variations were made but none of the compounds showed any useful crop selectivities.

Key words: sulfonylureas, herbicides, synthesis, 1,4-benzoxazin-3-ones, 1,4-benzothiazin-3-ones.

1 INTRODUCTION

The sulfonylurea herbicides discovered in the 1970s are the most active of all known classes of herbicide.[1] In addition to their remarkably low use-rates, sulfonylurea herbicides of varying structural types display a wide range of useful crop selectivities. It has been shown in many cases that sulfonylurea selectivity is the result of more rapid degradation of the herbicide in the crop than in the weed species.[2]

In nearly all commercial sulfonylureas the sulfonyl group is attached to an aromatic ring which has an *ortho*-substituent. It is also well known that high activity can be obtained with certain 2,3-disubstituted aromatic sulfonylureas and the related bicyclic systems **1a** (see Fig. 1 for structures).[3] Indeed quite a few bicyclic sulfonylurea systems have been patented,[4] and useful rice selectivity has been found in the case of the imidazo[1,2-*a*]pyridine sulfonylurea **1b**.[5]

* To whom correspondence should be addressed at: Biota Laboratory, Department of Chemistry, Monash University, Clayton, Victoria, Australia, 3168.

The 1,4-benzoxazin-3-one and 1,4-benzothiazin-3-one ring systems are readily accessible and appear to possess several sites which could undergo selective metabolism in crop plants. The preparation and screening was therefore undertaken of a series of novel sulfonylureas with the general structures **2** and **3** (Fig. 1) which incorporate examples of the above two ring systems attached to the sulfonylurea bridge.[6–8] It was noted that other workers had successfully used the 1,4-benzoxazin-3-one ring system to achieve crop selectivity in a different area of herbicide chemistry.[9]

2 EXPERIMENTAL METHODS

2.1 Synthesis of compounds

The compounds prepared are shown in Tables 1 and 2. The sulfonylureas **2** and **3** were generally prepared by reaction of the bicyclic sulfonamides of general structure **4a**, **4b** or **4c** with the phenyl carbamate **5** of the appropriate 2-aminopyrimidine (Fig. 2). The 3-oxo-1,4-benzoxazine-8-sulfonamides **4a** were generally prepared

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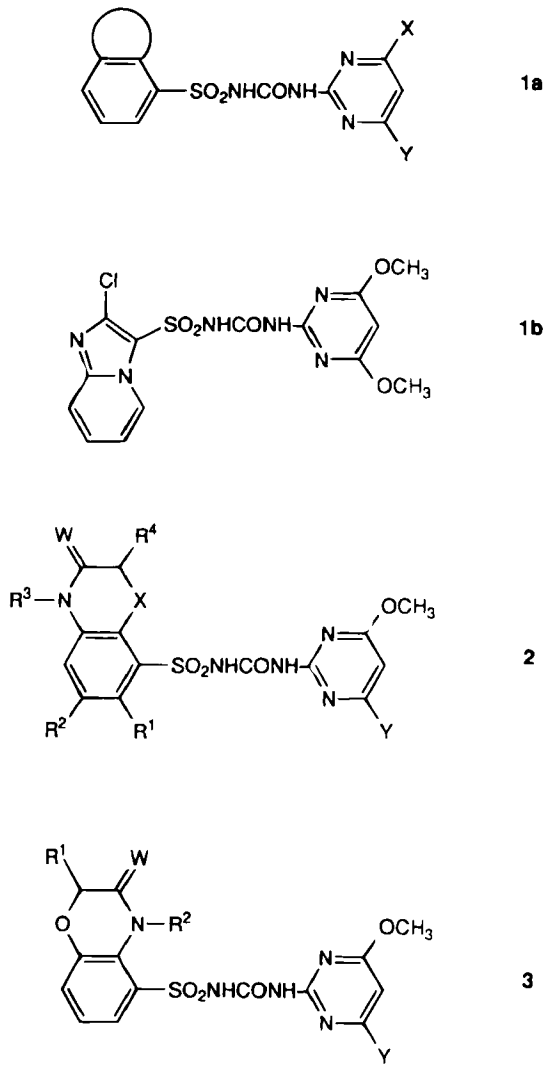


Fig. 1. Sulfonylurea herbicides.

by nitration of a suitable 2-chlorosulfonylphenol derivative and then ring formation by standard methods.[10] 3-Oxo-1,4-benzothiazine-8-sulfonamides **4b** were prepared by diazotisation of the corresponding 8-amino-1, 4-benzothiazinones using standard conditions.[11] Similarly, 3-oxo-1,4-benzoxazine-5-sulfonamides **4c** were prepared from the corresponding 5-amino derivatives by diazotisation. A representative synthetic procedure for each type of sulfonamide and for the sulfonylurea formation step is described below. All of the sulfonylureas prepared during this study were colourless or near colourless solids with moderate to high melting points. It was found that the best method for testing the purity of the compounds was [^{1}H]NMR spectroscopy (recorded at 200 MHz) which readily detected the presence of either starting material. The purity was also confirmed by thin layer chromatography (e.g., silica, ethyl acetate) and where appropriate by infra-red spectroscopy.

2.1.1 Intermediate sulfonamides

*Procedure A: preparation of 3,4-dihydro-3-oxo-2H-1,4-benzoxazine-8-sulfonamide (**4a**: $R^1 = R^2 = R^3 = R^4 = H$, $W = O$).* A solution of 5-bromo-2-hydroxybenzenesulfonylchloride (50 g) in dichloromethane (200 ml) was added dropwise to a cooled, stirred mixture of concentrated nitric acid (20 ml) and concentrated sulfuric acid (20 ml). The mixture was then allowed to come to room temperature and was stirred for a further 2 h. The reaction was quenched with ice-water and the organic layer was separated and dried over magnesium sulfate. The dried solution was cooled to 5°C and *tert*-butylamine (50 ml) was added dropwise with stirring. After 2 h at room temperature the reaction mixture was shaken with dilute citric acid solution and the organic layer was separated, dried and concentrated to give 5-bromo-2-hydroxy-3-nitro-*N*-*tert*-butylbenzenesulfonamide as a yellow solid (19 g, 29%).

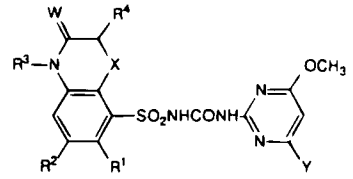
A solution of the *N*-*tert*-butylsulfonamide (7·1 g) and ammonium formate (10 g) in methanol (70 ml) was stirred, cooled in an ice bath and kept under nitrogen for 15 min before the addition of 10% palladium on charcoal (0·70 g). The mixture was then stirred at room temperature for 18 h. The mixture was filtered to remove the catalyst and the filtrate was concentrated to give crude 3-amino-2-hydroxy-*N*-*tert*-butylbenzene- sulfonamide as a dark oil (5·7 g).

Chloroacetyl chloride (6·7 ml) was added slowly to an ice-cooled mixture of sodium hydrogen carbonate (14·6 g) and the above amino-sulfonamide (15·5 g) in water (45 ml) and isobutyl methyl ketone (45 ml). The mixture was allowed to come to room temperature, stirred for 2 h and then heated under reflux for 4 h. Concentration of the reaction mixture under reduced pressure and trituration of the residue with ethyl acetate (200 ml) gave a solid which was collected by filtration. After washing with water 3,4-dihydro-3-oxo-*N*-*tert*-butyl-2*H*-1,4-benzoxazine-8-sulfonamide was obtained as a pale grey solid (10·1 g, 56%).

Treatment of the *tert*-butylsulfonamide with trifluoroacetic acid for 2 h at 60–70°C gave, in nearly quantitative yield, 3,4-dihydro-3-oxo-2*H*-1,4-benzoxazine-8-sulfonamide as a white solid [^{1}H]NMR (hexadeuterodimethyl sulfoxide) δ: 4·68 (s, 2H); 6·9–7·4 (m, 3H); 7·26 (s, 2H); 10·9 (s, 1H).

*Procedure B: preparation of 6-chloro-3,4-dihydro-3-oxo-2H-1,4-benzothiazine-8-sulfonamide (**4b**; $R^1 = R^3 = R^4 = H$, $R^2 = Cl$, $W = O$).* Thioglycolic acid (12·3 ml) was added to a stirred suspension of sodium carbonate (41 g) and 1,4-dichloro-2,6-dinitrobenzene (40 g) in ethanol (1000 ml). The suspension was stirred at room temperature for 16 h, acidified with concentrated hydrochloric acid and extracted with diethyl ether (3 × 300 ml). The combined ether extracts were washed with saturated sodium chloride solution, dried over sodium sulfate and concentrated to afford 4-chloro-2,6-

TABLE 1
Structures of 1,4-Benzoxazin-3-one and 1,4-Benzothiazin-3-one Sulfonylureas linked at the 8 Position



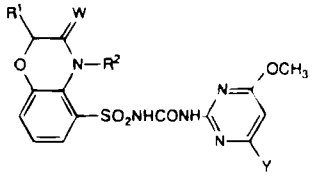
Compound	R^1	R^2	R^3	R^4	*W*	*X*	*Y*
2a	H	H	H	H	O	O	CH_3
2b	OCH_3	H	H	H	O	O	OCH_3
2c	CH_3	H	H	H	O	O	CH_3
2d	$CO_2C_2H_5$	H	H	H	O	O	OCH_3
2e	H	Cl	H	H	O	O	CH_3
2f	H	CH_3	H	H	O	O	CH_3
2g	CH_3	CH_3	H	H	O	O	OCH_3
2h	H	H	CH_3	H	O	O	CH_3
2i	H	H	H	CH_3	O	O	OCH_3
2j	H	F	H	CH_3	O	O	OCH_3
2k	H	H	CH_3	CH_3	O	O	CH_3
2l	H	H	CH_3	CH_3	S	O	CH_3
2m	H	F	CH_3	CH_3	O	O	OCH_3
2n	H	H	CH_3	H	S	O	CH_3
2o	H	H	H	CH_3	S	O	CH_3
2p	H	Cl	H	H	O	S	CH_3
2q	H	H	CH_3	CH_3	O	S	CH_3
2r	H	H	H	CH_3	O	S	CH_3
2s	H	H	H	H	O	SO	CH_3
2t	H	H	H	H	O	SO_2	CH_3
2u	H	H	H	H	H_2	O	CH_3
2v	H	H	CH_3	H	H_2	O	CH_3
2w	H	H	$COCH_3$	H	H_2	O	CH_3
2x	H	H	H	H	H_2	S	CH_3
2y	H	H	H	H	H_2	SO	CH_3
2z	H	H	H	H	H_2	SO_2	OCH_3
2aa	H	Cl	H	H	H_2	SO_2	CH_3
2bb	H	H	CH_3	CH_3	H_2	S	CH_3

dinitrophenylthioacetic acid as an orange solid (47 g, 95%).

Concentrated hydrochloric acid (450 ml) was added slowly and with ice-cooling to a solution of the substituted phenylthioacetic acid (32·6 g) and powdered tin metal (90 g) in ethanol (60 ml). The orange reaction mixture was heated under reflux until it became colourless (2 h) and then allowed to cool to room temperature. The colourless solution was poured slowly, with stirring, into ice-cold 40% aqueous sodium hydroxide (700 ml) and stirring was continued for another 0·25 h. The resulting cloudy suspension was extracted with ethyl acetate (3 × 300 ml) and the combined extracts washed with saturated sodium chloride solution. The organic layer was filtered through a pad of Celite, dried over sodium sulfate and evaporated to give 8-amino-6-chloro-3,4-dihydro-2*H*-1,4-benzothiazin-3-one as a colourless solid (18·6 g, 78%).

A solution of sodium nitrite (7·23 g) in water (10 ml) was added slowly to an ice-cold suspension of 8-amino-6-chloro-3,4-dihydro-2*H*-1,4-benzothiazin-3-one (18 g) in concentrated hydrochloric acid (200 ml) and acetic acid (37 ml). After stirring for 0·5 h at 0°C the golden brown solution of the diazonium salt was added slowly to a cooled, sulfur-dioxide-saturated solution of cuprous chloride (3·0 g) in concentrated hydrochloric acid (100 ml) and acetic acid (100 ml). The solution was allowed to warm to room temperature and stirred for a further 2 h before being diluted with water (1000 ml) and filtered. The solid was rinsed with cold water and dried to give the crude sulfonyl chloride as a brown solid (22 g). Concentrated aqueous ammonia (300 ml) was added slowly to a stirred suspension of the sulfonyl chloride in diethyl ether, (200 ml). The solution was then heated to boiling for 2 h to remove the ether, cooled and filtered to afford 6-chloro-3,4-dihydro-3-

TABLE 2
1,4-Benzoxazin-3-one Sulfonylureas linked at the 5-position



Compound	R^1	R^2	*W*	*Y*
3a	H	CH_3	O	OCH_3
3b	H	CH_3	O	CH_3
3c	H	C_2H_5	O	OCH_3
3d	H	C_2H_5	O	CH_3
3e	H	n-C_3H_7	O	CH_3
3f	H	CH_3	S	CH_3
3g	CH_3	CH_3	O	OCH_3
3h	CH_3	CH_3	O	CH_3

oxo-2*H*-1,4-benzothiazine-8-sulfonamide, as a pale brown solid (16·6 g, 71%). [^{1}H]NMR (hexadeuterodimethyl sulfoxide) δ: 3·58 (s, 2H); 7·20 (d, J = 2·2 Hz, 1H); 7·52 (d, J = 2·2 Hz, 1H); 7·66 (s, 2H); 10·98 (s, 1H).

Procedure C: preparation of 3,4-dihydro-4-methyl-3-oxo-2H-1,4-benzoxazine-5-sulfonamide (4c; $R^1 = H$, $R^2 = CH_3$, $W = O$). 3,4-Dihydro-5-nitro-2*H*-1,4-benzoxazin-3-one was prepared by the reaction of 2-amino-3-nitrophenol with chloroacetyl chloride using the standard conditions[10] and methylation with dimethylsulfate gave 3,4-dihydro-4-methyl-5-nitro-2*H*-1,4-benzoxazin-3-one in high overall yield. Under an atmosphere of nitrogen, palladium on charcoal (10%, 0·96 g) was added to a stirred mixture of the latter compound (3·31 g) and ammonium formate (6·0 g) in dry methanol. The mixture was stirred at room temperature for 4 h and then the catalyst was removed by filtration. The filtrate was evaporated under reduced pressure and the residue was taken up in ethyl acetate and washed with water. Evaporation of the organic layer gave 5-amino-3,4-dihydro-4-methyl-2*H*-1,4-benzoxazin-3-one as a waxy colourless solid (2·71 g, 95%). Diazotisation of the latter compound (7·43 g) using the normal conditions[11] gave 3,4-dihydro-4-methyl-3-oxo-2*H*-1,4-benzoxazine-5-sulfonamide as a pale brown solid (3·95 g, 39%). [^{1}H]NMR (hexadeuteroacetone-hexadeuterodimethyl sulfoxide) δ: 3·50 (s, 3H); 4·57 (s, 2H); 7·2–7·3 (m, 2H); 7·7–7·9 (m, 3H).

2.1.2 *Sulfonylurea formation*

*Procedure D: preparation of the sulfonylurea 1-(4-methoxy-6-methyl-pyrimidin-2-yl)-3-(3,4-dihydro-4-methyl-3-oxo-2H-1,4-benzoxazin-5-sulfonyl)urea, **3b**.* Compound **4c** (1·16 g) in dry tetrahydrofuran (20 ml) was treated dropwise with 1,8-diazabicyclo[5·4·0] undec-7-ene (1·05 ml) and the resultant solution was stirred at room temperature for 0·5 h. Phenyl *N*-(4-methoxy-6-methyl-2-pyrimidinyl)carbamate (1·36 g) was added and stirring was continued for 4 h. The reaction mixture was poured into ice-cold dilute aqueous citric acid (100 g litre^{-1}, 150 ml) and extracted with ethyl acetate (2 × 100 ml). The combined organic layers were washed with water, dried and evaporated. The residue was triturated with ether and the product **3c** collected by filtration (1·19 g, 61%). [^{1}H]NMR (hexadeuterodimethyl sulfoxide) δ: 2·39 (s, 3H); 3·47 (s, 3H); 3·93 (s, 3H); 4·60 (s, 2H); 6·59 (s, 1H); 7·15–7·45 (m, 2H); 7·87 (dd, J = 7·6, 2·2 Hz, 1H); 10·84 (s, 1H); 13·97 (br s 1H). [^{1}H]NMR data for other compounds synthesised are given in Table 3.

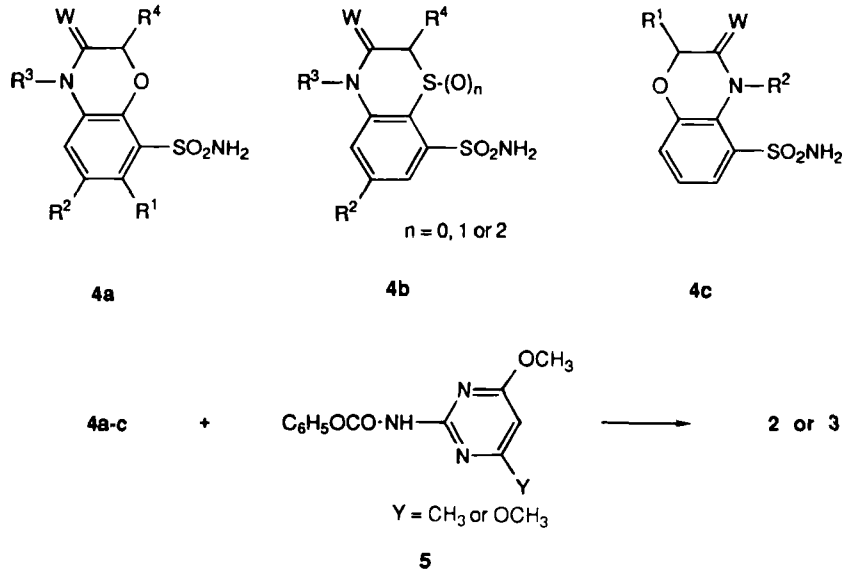


Fig. 2. Intermediates and general synthetic route.

TABLE 3
NMR Data of Compounds **2** and **3**

Compound	*[1H]NMR (δ ppm, in hexadeuterodimethyl sulfoxide unless otherwise stated)*
2a	2·34 (s, 3H), 3·54 (s, 1H), 3·94 (s, 3H), 4·51 (s, 2H), 6·54 (s, 1H), 6·91–7·50 (m, 3H), 10·5 (s, 1H), 11·1 (s, 1H)
2b	($CDCl_3$) 3·51 (s, 3H), 3·69 (s, 6H), 4·24 (s, 2H), 5·51 (s, 1H), 6·32 (d, 1H), 6·83 (d, 1H), 9·26 (s, 1H), 10·35 (s, 1H), 12·56 (s, 1H)
2c	($CDCl_3$) 2·30 (s, 3H), 3·60 (s, 6H), 4·07 (s, 2H), 5·46 (s, 1H), 6·52 (d, 1H), 6·69 (d, 1H), 9·40 (s, 1H), 10·45 (s, 1H), 12·48 (s, 1H)
2d	($CDCl_3$) 1·40 (t, 3H), 2·45 (s, 3H), 3·96 (s, 3H), 4·41 (q, 2H), 4·54 (s, 1H), 6·34 (s, 1H), 7·25 (d, 1H), 7·54 (d, 1H), 9·6 (s, 1H), 9·95 (s, 1H)
2e	2·41 (s, 3H), 3·94 (s, 3H), 4·61 (s, 2H), 6·58 (s, 1H), 7·12 (d, 1H), 7·36 (d, 1H), 10·5 (br s, 1H), 11·1 (br s, 1H), 13·2 (br s, 1H)
2f	2·30 (s, 3H), 2·44 (s, 3H), 3·94 (s, 3H), 4·40 (s, 2H), 6·30 (s, 1H), 6·94 (s, 1H), 7·33 (s, 1H), 9·6 (s, 1H), 10·7 (s, 1H), 13·1 (s, 1H)
2g	2·2 (s, 3H), 2·4 (3H), 3·89 (s, 6H), 4·4 (s, 2H), 5·96 (s, 1H), 6·93 (s, 1H), 10·1 (s, 1H), 10·7 (s, 1H), 12·5 (s, 1H)
2h	($CDCl_3$) 2·4 (s, 3H), 3·3 (s, 3H), 3·9 (s, 3H), 4·6 (s, 2H), 6·3 (s, 1H), 7·1–7·4 (m, 2H), 7·7–7·9 (m, 1H) (NH not observed)
2i	1·3 (d, 3H), 3·8 (s, 6H), 4·7 (q, 1H), 5·7 (s, 1H), 6·9–7·6 (m, 3H), 9·1 (s, 1H), 10·8 (s, 1H), 12·9 (s, 1H)
2j	1·26 (d, 3H), 3·91 (s, 6H), 4·77 (q, 1H), 6·01 (s, 1H), 7·1–7·8 (m, 2H), 10·63 (s, 1H), 11·1 (br s, 1H), 12·9 (br s, 1H)
2k	1·4 (d, 3H), 2·4 (s, 3H), 3·4 (s, 3H), 3·9 (s, 3H), 4·7 (q, 1H), 6·5 (s, 1H), 7·0–7·8 (m, 3H), 9·2 (s, 1H), 13·2 (s, 1H)
2l	1·4 (d, 3H), 2·5 (s, 3H), 3·9 (s, 3H), 4·0 (s, 3H), 5·2 (q, 1H), 6·5 (s, 1H), 7·1–7·9 (m, 3H), 9·3 (br s, 1H), 13·3 (br s, 1H)
2m	1·27 (d, 3H), 3·30 (s, 3H), 3·89 (s, 3H), 4·80 (q, 1H), 6·01 (s, 1H), 7·37 (m, 2H), 10·6 (br s, 1H), 12·8 (br s, 1H)
2n	2·5 (s, 3H), 3·8 (s, 3H), 3·9 (s, 3H), 4·9 (s, 2H), 6·3 (s, 1H), 6·9–8·0 (m, 3H) (NH not observed)
2o	1·5 (d, 3H), 2·5 (s, 3H), 4·0 (s, 3H), 5·1 (q, 1H), 6·5 (s, 1H), 6·9–7·9 (m, 3H), 9·3 (s, 1H), 11·7 (s, 1H), 13·3 (s, 1H)
2p	2·4 (s, 3H), 3·5 (s, 2H), 3·9 (s, 3H), 6·5 (s, 1H), 7·3 (d, 1H), 7·6 (d, 1H), 10·9 (br s, 1H), 12·5 (br s, 1H)
2q	1·0 (d, 3H), 2·3 (s, 3H), 3·3 (s, 3H), 3·5 (q, 1H), 3·9 (s, 3H), 6·5 (s, 1H), 7·5–7·8 (m, 3H), 10·6 (br s, 1H), 13·7 (br s, 1H)
2r	1·0 (d, 3H), 2·5 (s, 3H), 3·5 (q, 1H), 3·9 (s, 3H), 6·5 (s, 1H), 7·2–7·8 (m, 3H), 10·5 (s, 1H), 10·9 (br s, 1H), 13·7 (br s, 1H)
2s	2·41 (s, 1H), 3·93 (s, 3H), 4·17 (s, 2H), 6·58 (s, 1H), 7·0–7·9 (m, 3H), 10·7 (s, 1H), 11·2 (s, 1H), 14·0 (br s, 1H)
2t	2·38 (s, 3H), 3·94 (s, 3H), 4·83 (s, 2H), 6·53 (s, 1H), 7·10–7·95 (m, 3H), 10·61 (s, 1H), 11·42 (s, 1H), 13·5 (br s, 1H),
2u	($d_6$acetone) 2·4 (s, 3H), 3·4 (m, 2H), 3·9 (s, 3H), 4·1 (m, 2H), 6·7–7·3 (m, 3H), 9·1 (s, 1H), 11·2 (s, 1H), 13·0 (s, 1H)
2v	2·4 (s, 3H), 2·9 (s, 3H), 3·3 (m, 2H), 3·9 (s, 3H), 4·2 (m, 2H), 6·5 (s, 1H), 6·7–7·4 (m, 3H), 9·8 (br s, 1H), 13·0 (br s, 1H)
2w	2·2 (s, 3H), 2·4 (s, 3H), 3·9 (m, 5H), 4·3 (m, 2H), 6·5 (s, 1H), 6·9–8·3 (m, 3H), 10·3 (br s, 1H), 13·2 (br s, 1H)
2x	2·39 (s, 3H), 2·78 (m, 2H), 3·40 (m, 2H), 3·95 (s, 3H), 6·51 (s, 1H), 6·6–7·5 (m, 4H), 10·45 (s, 1H), 13·26 (br s, 1H)
2y	2·38 (s, 3H), 3·04 (m, 2H), 3·64 (m, 2H), 3·94 (s, 3H), 6·52 (s, 1H), 6·9–7·4 (m, 3H), 10·45 (s, 1H), 13·75 (br s, 1H)
2z	3·45 (s, 2H), 3·67 (m, 2H), 3·95 (s, 6H), 5·90 (s, 1H), 6·9–7·4 (m, 3H), 10·65 (br s, 1H), 12·75 (br s, 1H)
2aa	2·37 (s, 3H), 3·49 (m, 2H), 3·66 (m, 2H), 3·95 (s, 3H), 6·51 (s, 1H), 7·18 (d, 1H), 7·30 (d, 1H), 7·75 (s, 1H), 10·57 (s, 1H), 13·32 (s, 1H)
2bb	1·04 (d, 3H), 2·39 (s, 3H), 2·95 (s, 3H), 3·17 (m, 2H), 3·60 (m, 1H), 3·95 (s, 3H), 6·55 (s, 1H), 6·9–7·4 (m, 3H), 10·49 (s, 1H), 13·39 (s, 1H)
3a	3·92 (s, 6H), 4·76 (s, 2H), 6·00 (s, 2H), 7·1–7·7 (m, 3H), 9·65 (s, 1H), 10·72 (s, 1H),
3b	2·39 (s, 3H), 3·47 (s, 3H), 3·93 (s, 3H), 4·60 (s, 2H), 6·59 (s, 1H), 7·15–7·45 (m, 2H), 7·87 (dd, 1H), 10·84 (s, 1H), 13·97 (br s, 1H)
3c	0·87 (t, 3H), 3·91 (s, 6H), 4·23 (q, 2H), 4·52 (s, 2H), 5·99 (s, 1H), 7·2–7·55 (m, 2H), 7·85 (dd, 1H), 10·31 (s, 1H) (one NH not observed)
3d	0·84 (t, 3H), 2·40 (s, 3H), 3·94 (s, 3H), 4·28 (q, 2H), 4·49 (s, 2H), 6·61 (s, 1H), 7·2–7·45 (m, 2H), 7·86 (dd, 1H), 10·92 (s, 1H), 13·93 (s, 1H)
3e	0·63 (t, 3H), 1·31 (m, 2H), 2·46 (s, 3H), 3·97 (s, 3H), 4·29 (t, 2H), 4·54 (s, 2H), 6·55 (s, 1H), 7·2–7·5 (m, 2H), 7·95 (dd, 1H), 10·60 (s, 1H), 14·0 (s, 1H)
3f	2·45 (s, 3H), 3·94 (s, 3H), 3·97 (s, 3H), 4·85 (s, 2H), 6·55 (s, 1H), 7·3–7·45 (m, 2H), 7·97 (dd, 1H), 10·64 (br s, 1H), 14·04 (br s, 1H)
3g	1·44 (d, 3H), 3·45 (s, 3H), 3·91 (s 6H), 4·61 (q, 1H), 6·00 (s, 1H), 7·05–7·5 (m, 2H), 7·86 (dd, 1H), 10·51 (br s, 1H) (one NH not observed)
3h	1·43 (d, 3H), 2·39 (s, 3H), 3·46 (s, 3H), 3·93 (s, 3H), 4·50 (q, 1H), 6·59 (s, 1H), 7·0–7·45 (m, 2H), 7·65 (dd, 1H), 10·85 (s, 1H), 13·72 (s, 1H)

TABLE 4
Post-Emergent Herbicidal Activity of Compounds of General Structure **2** & **3** on Various Crop and Weed Plant Species[a]

Compound No.	*Rate g ha*$^{-1}$	*Phytoxicity (%)*										
		Sy	*Ma*	*Ri*	*Wh*	*Ga*	*Ab*	*Ip*	*Av*	*Se*	*Ec*	*Cy*
2a	25	65	85	65	65	—	65	15	65	65	85	35
2b	25	95	65	10	30	95	65	85	95	65	95	20
2b	5	85	50	10	20	75	65	75	95	50	95	—
2c	25	20	95	75	65	—	0	20	95	50	85	20
2d	25	30	75	50	75	85	50	0	75	0	85	0
2e	25	65	35	15	65	65	65	35	85	15	65	15
2f	25	85	65	35	65	65	65	65	65	35	85	35
2g	25	65	65	15	35	15	65	0	65	35	35	65
2h	25	65	65	35	65	65	65	35	85	65	65	35
2i	18	65	65	35	65	85	65	65	85	65	85	35
2j	25	65	35	35	65	65	65	35	85	35	85	65
2k	25	35	85	85	65	65	65	65	85	65	85	15
2l	25	35	65	65	65	15	15	65	65	15	35	35
2m	25	35	35	35	65	35	35	35	65	35	65	15
2n	125	35	65	15	85	65	35	15	15	85	65	15
2o	25	65	65	65	65	65	65	65	35	35	65	35
2p	125	65	65	0	35	35	35	0	65	0	65	15
2q	25	65	65	35	65	85	0	0	85	0	85	65
2r	25	85	65	15	65	65	65	65	85	35	65	65
2s	125	65	65	15	65	85	65	65	85	65	65	15
2t	125	98	15	0	0	15	0	0	0	35	0	0
2u	25	35	85	15	65	85	65	85	85	35	85	65
2u	5	15	65	0	65	85	15	65	65	15	85	0
2v	25	35	65	15	65	65	65	65	35	65	65	65
2w	25	65	85	35	65	15	65	35	65	65	85	65
2x	25	85	65	15	65	35	65	65	65	65	65	0
2y	25	85	65	15	65	65	65	65	65	15	65	15
2z	125	98	98	35	85	98	85	85	98	98	98	35
2aa	25	35	0	35	0	35	15	35	0	15	15	0
2bb	25	85	85	15	65	65	15	65	35	0	15	15
3a	25	85	0	15	35	65	35	65	15	35	35	65
3a	125	85	0	15	15	85	85	65	65	65	85	85
3b	25	0	35	15	65	85	35	15	0	85	85	65
3b	125	0	85	85	85	98	65	65	65	85	85	85
3c	25	0	10	0	0	10	65	20	0	0	0	0
3d	25	0	0	20	3	30	50	50	0	0	65	0
3e	25	0	15	0	0	0	65	65	0	0	0	0
3f	25	0	35	15	65	15	0	35	35	0	15	15
3g	25	35	0	15	15	65	35	15	35	15	15	35
3h	25	15	0	15	0	65	35	65	65	15	35	15
Bensulfuron-methyl	125	95	50	0	10	95	75	65	0	0	75	50
Chlorsulfuron	5	85	65	10	10	95	75	75	0	30	75	0
Chlorimuron-ethyl	5	20	50	20	10	85	30	50	20	10	85	75

[a] Code for crop and weed species: Sy-Soybean; Ma-Maize; Ri-Rice; Wh-Wheat; Ga-*Galium aparine* L.; Ab-*Abutilon theophrasti* (L.) Medic; Ip-*Ipomoea purpurea* (L.) Roth.; Av-*Avena fatua* L.; St-*Setaria viridis* (L.) Beauv.; Ec-*Echinochloa crus-galli* (L.) Beauv.; Cy-*Cyperus rotundus* L.

2.2 Biological evaluation

All of the compounds reported in Tables 1 and 2 were tested under glasshouse conditions for herbicidal activity against seven crop species and a variety of weed species and a summary of the results is given in Table 4. The growing conditions in the glasshouse for all tests were a 14-h daylight period using mercury vapour lamps, day temperatures of 24°C and night temperatures of 19°C.

The compounds were formulated for test by mixing an appropriate amount with 5 ml of an emulsion prepared by diluting 160 ml of a solution containing 'Span' 80 (21·9 g litre^{-1}) and 'Tween' 20 (78·2 g litre^{-1}) in methylcyclohexanone to 500 ml with water. The formulation used was selected because it did not cause any phytotoxicity to the plants and blank formulations were periodically sprayed to check this. Each 5 ml emulsion containing a test compound was diluted to 40 ml with water and sprayed onto young pot plants of the species named in Table 4.

The sprayer volume used in all glasshouse tests was 1000 litre ha^{-1} and the soil type was a 50% loam/50% grit mixture, supplemented by a slow-release fertiliser. The growth stage of the plants (all crops and weeds) was two to four leaves at the time of spraying. Damage to test plants was assessed after 13 days as a percentage phytotoxicity. On occasions test plants were left for longer than 13 days, but the final assessment at 20 days was seldom very different from that at 13 days. Three standards, chlorsulfuron, bensulfuron-methyl and chlorimuron-ethyl were included in all tests to calibrate the screens. Typical results for the three standards are also given in Table 4. It should be noted that bensulfuron and chlorimuron are normally used pre-emergence and, while they provide a useful benchmark, they do not perform perfectly in a post-emergence treatment. The degree of phytotoxicity was assessed by comparison with untreated control plants. A dash (—) means that no experiment was carried out.

3 RESULTS AND DISCUSSION

3.1 Synthesis of compounds

There are no reported examples of 1,4-benzoxazin-3-ones or 1,4-benzothiazin-3-ones with a sulfonamide functionality at either the 5 or the 8 position. We have now developed general methods for the preparation of 8-sulfonamides of type **4a** which involve introduction of the sulfonyl group *ortho* to the oxygen atom by chlorosulfonation of a suitable, optionally protected, phenol. The protecting groups are then removed and the benzoxazinone ring system is formed as the last stage of the sequence. For the preparation of the 5-sulfonamides **4c**, 2-amino-3-nitrophenol was used as starting material, the benzoxazinone ring was formed and then diazotisation was used to introduce the sulfonamide group.

The 8-sulfonamido 1,4-benzothiazin-3-ones of structure **4b** were prepared starting from a suitable 4-substituted 1-chloro-2,6-dinitrobenzene. The activated chlorine atom allows easy introduction of sulfur using thioglycolic acid and, upon reduction of the nitro groups, the benzothiazinone ring system is formed. Diazotisation of the second amino group then allows introduction of the sulfonamido functionality, generally in reasonable overall yield.

Many of the novel sulfonamides of type **4a–4c** were coupled to a variety of 2-aminopyrimidines and 2-aminotriazines to form several final sulfonylureas. It was found that the 4,6-dimethoxy and 4-methoxy-6-methyl pyrimidines gave by far the most active sulfonylureas and only compounds of this class are discussed here.

3.2 Herbicidal activity

At the outset of our work on bicyclic sulfonylureas the primary aim was to find a compound with broad-spectrum post-emergent activity, but selective to wheat and barley. The first 1,4-benzoxazin-3-one sulfonylurea which was made and tested was the parent compound **2a** which showed an encouraging level of activity, although no sign of any crop selectivity. The introduction of an *ortho* substituent on the aromatic ring, as in compounds **2b–d**, maintained a high level of activity and **2b**, with a 7-methoxy group, showed promising signs of rice selectivity. Substitution at the *meta* or 6-position, such as with compounds **2e–g**, tended to reduce the overall activity. Benzoxazinones with an alkyl group on either the ring nitrogen (**2h** and **2k–2n**) or the 2-position (**2i–j** and **2o**) all showed moderate levels of activity, but again no strong signs of crop safety.

The benzothiazinone sulfonylureas **2p–2t** generally showed lower levels of activity than the corresponding benzoxazinones. Compounds **2u–2bb** in which the ring carbonyl group has been reduced showed good levels of activity, with **2u** and **2z** giving some signs of rice selectivity.

The 5-linked benzoxazinones **3a–3h** were generally not as active as the 8-linked series. The activity dropped off sharply with increasing size of the nitrogen substituent R^2, with the ethyl and propyl compounds **3c–3e** being almost inactive. The *N*-methyl compounds **3a** and **3b**, however, showed interesting signs of maize and soybean selectivity, but were not sufficiently active to be of really high interest.

In summary, all three series of novel bicyclic sulfonylureas showed moderate levels of activity and a few of the compounds tested gave some signs of crop selectivity. Whilst several compounds were investigated

more fully in the glasshouse, none of the compounds was considered to be worthy of detailed field evaluation.

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